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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/595,682	06/16/2000	Mary K. Danks	SJ-0005	1625

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EXAMINER	
QIAN, CELINE X	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

S.A.M.

Advisory Action	Application No. 09/595,682	Applicant(s) DANKS ET AL.	
	Examiner Celine X Qian	Art Unit 1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 December 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will not be entered because:
   (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ they raise the issue of new matter (see Note below);
   (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: *See Continuation Sheet*.
3. ☐ Applicant's reply has overcome the following rejection(s): _____.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *12-14,18 and 22-29*.

   Claim(s) withdrawn from consideration: _____.
8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.
10. ☐ Other: _____

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER

Continuation of 2. NOTE: The newly added claim 30 does not overcome the 112 1st paragraph rejection (both scope of enablement and written description) of the record. Furthermore, the method of claim 30 only recites administration of a CE-encoding polynucleotide, and no prodrug is administered; thus, tumor growth would not be inhibited. Moreover, the amended claim 18 raises new issues under written description. Claim 18 recites "a rabbit carboxylesterase capable of cleaving a chemotherapeutic prodrug APC or CPT-11 and inactive metabolites thereof..." The specification only disclose one specific rabbit carboxylesterase that is able to cleave APC or CPT-11. In addition, the specification discloses that the only inactive metabolite of CPT-11 is APC, which is cleavable by the carboxylesterase. The specification fails to disclose that other inactive metabolite of CPT-11, or any inactive metabolite of APC that is cleavable by the rabbit carboxylesterase. Therefore, the amendment creats new issues of written description. Lastly, the amendment also raises new 112 2nd paragraph issue for claims 23, 24, 25 and 27. Claims 23 and 24 recite "the carboxylesterase comprises a rabbit carboxylesterase," which renders the claim indefinite because it is unclear what is the nature of such carboxylesterase. Both claims 25 and 27 fail to limit the parent claim. Therefore, the proposed amendment will not be entered.

Continuation of 5. does NOT place the application in condition for allowance because: the proposed amendment does not overcome the 112 1st paragraph rejections raised in the previous actions mailed on 4/9/03 and 9/24/03. Claims 12, 13 and 22 are allowable because they are directed to sensitizing tumor cells in vitro. However, the newly added claim 30 still have 112 1st paragraph issue. In response to the rejection, Applicants argue that the Declaration 2 filed on 7/9/03 demonstrate a correlation between the CE expression and the asserted use of sensitizing tumor cells in vivo using vectors other than adenoviral vectors. Applicants argue that this evidence supports the enablement of the claims to the scope of using multiple gene delivery system in vivo. Applicants further argue that the Declaration 1 and 2 demonstrate the effectiveness of rabbit CE, human intestinal CE and bacterial CE expression for cleaving a prodrug. Further, Applicants argue that the specification teaches how to identify other type of CE. Applicnats thus conclude that the claim is enabled for the scope that encompasses any type of CE. These arguments are not persuasive. Contrary to Applicant's assertion, the office action mailed on 4/9/03 clearly discusses the unpredictability in the art of gene therapy (see pages 4-6), especially the route of delivery. The specification fails to teach how to overcome such unpredictability. Contrary to Applicant's assertion, Declaration 1 only demonstrate the effectiveness of rabbit CE delivered by adenoviral vector in vivo, and Declaration 2 provides only in vitro enzymatic activity of the bacterial, human intestinal and another human CE. As such, for same reasons discussed in the previous office actions, the scope of the enablement is limited to what is indicated in the office action mailed on 9/24/03.
In response to the written description requirement, applicants argue that the specification and the Declaration also disclose the human intestinal CE, the bacterial CE, and methods to identify such CE. Applicants further argue that there is no undue experimentation to identify other CE using the computer model and assays taught by the specification. These arguments are not peruasive. The written description requirement clearly state that the specification must describe the claimed genus by a representative number of species by their complete structure or other identifying characteristics. Such requirement has nothing to do with undue experimentation. The claimed genus "a carboxylesterase capable of cleaving APC or CPT-11 in vivo." The specification and the Declaration only disclosed 4 CE, and 3 of them cleaves CPT-11 effectively in vitro. Although the assay identifies the CE in vitro, it does not teach the structural and the functional relationship between the enzyme and its ability to cleave the drug. Therefore, the written description rejection would be applied to this claim if it is entered.
The proposed amendment also raises new issues under 112 1st and 2nd paragraph (see no.2 above). Therefore, the claims are not allowable.